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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JACQUES DEGELAEN, JEAN-MARIE FRERE, BENOIT GRANIER, and BERNARD JORIS

Appeal 2008-5883
Application 10/702,507
Technology Center 1600

Decided:[1] February 25, 2009

Before ERIC GRIMES, LORA M. GREEN, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 24, 26-32, and 34-40. We have jurisdiction under 35 U.S.C. § 6(b).

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

STATEMENT OF THE CASE

The claims are directed to an assay kit for detecting one or more antibiotics having a β-lactam ring. Claim 24 is representative of the claims on appeal, and reads as follows:

24. An assay kit for detecting one or more antibiotics containing a β-lactam ring in a liquid dairy product, said assay kit comprising:

(a) an assay device comprising a solid support, said solid support comprising (a) a first and second end, and (b) the following membranes (i)-(iii), fixed in succession starting from the first end,

(i) a purification membrane which retains interfering substance(s) and allows antibiotics and detection reagents in the liquid dairy product to migrate by tangential capillary migration from the first end towards the second end of the solid support, while preserving the activity of the antibiotics and detection reagents during said migration, said interfering substance(s) being substances which prevent such migration, said purification membrane being made from non-woven polyester fibers which is capable of retaining leukocytes in the milk,

(ii) an immobilization membrane comprising first and second capture substances, said first capture substance being one or more antibiotics containing a β-lactam ring which specifically bind to a receptor, which is a BlaR and BlaR-CTD protein obtained from *Bacillus lichenformis*, said second capture substance being a substance which binds to an independent reference substance, and

(iii)[2] an absorbent membrane,

(b) a detection reagent in the test kit comprising the receptor which is the BlaR and BlaR-CTD protein obtained from *Bacillus lichenformis* which specifically binds to antibiotics containing a β-lactam ring in the dairy product, and

(c) the independent reference substance.

The Examiner relies on the following evidence:

Markovsky	US 6,319,466	Nov. 20, 2001
Pall	US 6,074,869	Jun. 13, 2000

[2] The reference to (iv) in the claims on appeal attached to the Appeal Brief appears to be in error. (*See* Amendement dated April 18, 2007.)

Litman EP 0 093 613 Sep. 11, 1983

B. Joris et al., *Expression in Escherichia coli of the carboxy terminal domain of the BLAR sensory-transducer protein of Bacillus licheniformis as a water-soluble M_r 26 000 penicillin-binding protein*, 70 FEMS MICROBIOLOGY LETTERS, 107-114 (1990).

We affirm.

ISSUE (Obviousness)

The Examiner concludes that claims 24, 26-32, and 36-40 are rendered obvious by the combination of Markovsky, Joris, and Litman, and that claims 34 and 35 are rendered obvious by the combination of Markovsky, Joris, and Litman, as further combined with Pall.

Appellants contend that the combination is based on an "obvious to try" rationale, and that the Examiner engaged in hindsight reasoning.

Thus, the issue on Appeal is: Have Appellants demonstrated that the Examiner erred in combining the references to arrive at the claimed invention?

FINDINGS OF FACT

FF1 The Examiner rejects claims 24, 26-32, and 36-40 under 35 U.S.C. § 103(a) as being obvious over the combination of Markovsky, Joris, and Litman (Ans.[3] 4). As Appellants do not argue the claims separately, we

[3] All references to the Answer (Ans.) are to the Examiner's Answer dated December 17, 2007. We note that a Supplemental Examiner's Answer was sent out on May 15, 2008, but that Answer merely corrected minor informalities in the headings.

focus our analysis on claim 24, and claims 26-32 and 36-40 stand or fall with that claim. 37 C.F.R. § 41.37(c)(1)(vii).

FF2 The Examiner cites Markovsky for teaching all of the elements of claim 24 (Ans. 4-5), except for teaching the use of receptors obtained from *Bacillus lichenformis* as the labeled reagent or the use of a reference that is independent of the analyte (*id.* at 5).

FF3 The Examiner notes, however, that Markovsky teaches that "the receptor may bind a family of analytes which have similar structural binding sites," and also teaches that "test kits for detecting beta-lactams in biological fluids are well known in the art." (*Id.*)

FF4 The Examiner finds further that Markovsky teaches a lateral flow assay device for detecting β-lactam antibiotics, and the use of receptors that are specific to the analyte, thus it would be "entirely within the skills of the ordinary artisan to choose a receptor that is specific for the analyte." (*Id.* at 9.)

FF5 Specifically, Markovsky teaches the use of a labeled receptor that reacts with the analyte to form a receptor-analyte complex (Markovsky, col. 1, ll. 53-55), wherein the receptor may bind a family of analytes that have similar structural binding sites (*id.* at col. 2, ll. 11-13).

FF6 Markovsky specifically teaches an assay test strip for beta-lactam antibiotics in milk (*id.* at col. 8, ll. 13-15).

FF7 Markovsky also exemplifies the use of a beta-lactam receptor from *Bacillus stearothermophilus* (*id.* at col. 12, ll. 35-39).

FF8 The Examiner cites Joris for teaching that BLAR and BLAR-CTD are involved in the induction of β-lactamase in *Bacillus lichenformis* (Ans. 5 (*see* Joris Abstract)).

FF9 Joris teaches that BLAR-CTD, the carboxy-terminal domain of BLAR, is a water-soluble, penicillin binding protein (Joris Abstract).

FF10 The Examiner cites Litman for teaching "a method and device for detecting an analyte comprising a measurement surface and a calibration surface binding to a reagent independent from the analyte." (Ans. 6 (citing Litman 4, ll. 24-37).)

FF11 The Examiner concludes that it would have been obvious to the ordinary artisan to use the BLAR and BLAR-CTD receptors as taught by Joris in the device of Markovsky because Joris discloses that the BLAR and BLAR-CTD receptors are readily available and are known in the art as having β-lactamase activity, and thus the ordinary artisan "would have a reasonable expectation of success in using receptors BlaR and BlaR-CTD to detect beta-lactams antibiotics such as penicillin as taught by Markovsky." (Ans. 6.)

FF12 The Examiner concludes further that the use of an independent reference or calibration agent is well known in the art, and thus it would have been obvious to the ordinary artisan to use the calibration reagents and the method of Litman in the device of Markovsky because "Litman teaches that it is advantageous to use a reagent that is independent from the analyte to provide a calibration or reference signal such that a standard for evaluation of the analyte at the detection zone can be obtained." (*Id.* at 7.)

FF13 The Examiner also rejects claims 34 and 35 under 35 U.S.C. § 103(a) as being obvious over the combination of Markovsky, Joris, and Litman, as further combined with Pall (Ans. 7).

FF14 The combination of Markovsky, Joris, and Litman are relied upon as above (*id.*).

FF15 The Examiner notes that the combination fails to specifically disclose the pore size of the purification membrane (*id.*).

FF16 The Examiner cites Pall for teaching membranes for filtering biological samples, such as leukocytes and milk, wherein the membrane is a non-woven web (polyethylene) having an average pore size of 3 to 8 μm (*id.* (citing Pall, col. 8, ll. 54-60)).

FF17 The Examiner concludes that

> it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the purification membrane taught by Pall in the device of Markovsky as modified by Joris because such a membrane is well known in the art and provides the advantage of a substantially uniform porous medium that can separate large somatic cells from a biological sample.

(Ans. 8.)

PRINCIPLES OF LAW

The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) secondary considerations of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966).

The Supreme Court has recently emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, ___, 127 S. Ct. 1727, 1741 (2007). "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *Id.* at 1739. An "[e]xpress suggestion to substitute one equivalent for another need not be present to render such substitution obvious." *In re Fout*, 675 F.2d 297, 301 (CCPA 1982). As noted by the Supreme Court,

> If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.

KSR, 127 S.Ct. at 1740.

Moreover, "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated technical success, it is likely the product not of innovation but of ordinary skill and common sense." *Id.* at 1742.

ANALYSIS

Appellants argue that Markovsky teaches the use of a beta-lactam receptor from *Bacillus stearothermophilus* (BST), which was well known as a receptor, and that there is no description of another specific bacterial protein that may be used in the assay (App. Br.[4] 9). Given the large number of bacteria, Appellants argue that the ordinary artisan would not select the membrane receptor of claim 24 based on the teachings of Markovsky (Reply Br. 2).

Appellants assert that while Joris describes BLAR proteins that bind beta-lactam antibiotics, there is no discussion of their use in a lateral flow assay, and thus there is no way to determine from the reference that the proteins would be effective in determining beta-lactam antibiotics in such as an assay, or that they even would be able to flow in the assay (App. Br. 9-10).[5] According to Appellants, the Examiner's rejection is based on an "obvious to try" premise, but "[i]n a complex lateral flow assay as claimed, there would be no assurance that the BlaR or BlaR-CTD proteins would function in such an assay, since the complex with the antibiotic is subjected to lateral flow." (*Id.* at 10). Appellants argue further that the combination

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[4] All references to the Appeal Brief (App. Br.) are to the Supplemental Appeal Brief dated September 19, 2007.

[5] In the Reply Brief, Appellants raise the argument (which was not raised in the Appeal Brief) that Joris does not discuss that the receptor functions for a large number of antibiotics (Reply Br. 2). Claim 32, however, is drawn to an assay kit, and thus the recitation of which antibiotic is being tested for is a statement of intended use. In addition, as the combination uses the same labeled receptor as used by Appellants, the ability of that receptor to bind to the claimed Markush group of antibiotics would be an inherent property of that receptor.

"could not lead one skilled in the art to [the] claimed invention without hindsight." (Reply Br. 3-4).

We have considered Appellants' arguments, but do not find them to be convincing. Markovsky teaches a lateral flow assay for detecting β-lactam antibiotics in milk (FF4, FF6). Markovsky teaches the use of a labeled receptor that specifically binds the antibiotic in the test strip (FF3-FF5), and specifically exemplifies the use of a beta-lactam receptor from BST (FF7). We agree with the Examiner, however, that the ordinary artisan would understand that other receptors which specifically bind the analyte of interest would be useful in the assay and the device (*see* FF4). Joris teaches that the *Bacillus lichenformis* protein BLAR and BLAR-CTD (the carboxy-terminal domain of BLAR) specifically bind to penicillin (FF8, FF9). Thus, it would have been well within the level of skill in the art to substitute the BLAR or BLAR-CTD receptor of *Bacillus lichenformis* for the beta-lactam receptor from BST as exemplified by Joris, because each specifically recognizes a beta-lactam antibiotic.

We recognize that there are a large number of bacteria from which beta-lactam receptors may be obtained, but just because the group of obvious variants may be large does not make the use of any specific-binding protein for a beta-lactam antibiotic any less obvious. In addition, while Appellants argue that there is no assurance that the BLAR or BLAR-CTD-beta-lactam antibiotic will flow in the assay, Appellants have not provided any scientific reasoning or evidence that the ordinary artisan would not expect the complex to flow, especially given the different assays exemplified by Markovsky. Note that arguments of counsel cannot take the place of

evidence in the record. *In re Scarbrough*, 500 F.2d 560, 566 (CCPA 1974). Moreover, while there may not be one-hundred percent assurance that the assay will work with a different specific binding protein, that is not the standard by which obviousness is measured: All that is required is a reasonable expectation of success, not absolute predictability of success. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

Appellants argue further that while Litman teaches the use of a calibration surface that binds to a reagent that it is independent from the analyte, and while the use of such calibration is known, its use is not known in the claimed assay (App. Br. 10).

Appellants' arguments are again not found to be convincing. As found by the Examiner, the use of an independent reference or calibration agent is well known in the assay art, and Litman provides a reason for adding an independent reference or calibration agent by teaching that it is advantageous to use a reagent that is independent from the analyte to provide a calibration or reference signal such that a standard for evaluation of the analyte at the detection zone can be obtained (FF12). Moreover, Appellants have not provided any evidence or scientific reasoning as to why it would have been beyond the level of ordinary skill in the art to use a calibration surface that binds to a reagent that it is independent from the analyte as taught by Litman in the assay of Markovsky.

As to the rejection of claims 34 and 35 over the combination of Markovsky, Joris, and Litman, as further combined with Pall, Appellants reiterate their arguments as to the combination of Markovsky, Joris, and Litman (App. Br. 11-12). Appellants argue further that claims 34 and 35

require an 8 μm pore size, which is small, and contend that there is no suggestion in Pall that the BlaR or BlaR-CTD bound with antibiotics would pass through the web of Pall (*id.*).

We point Appellants' attention to the response to arguments set forth above. In addition, Markovsky teaches a use of membranes in the assay device for beta-lactam devices (*see, e.g.*, FF2), thus the ordinary artisan would have a reasonable expectation of success of using the membrane of Pall in the device of Markovsky (*see, e.g.*, Ans. 11).

CONCLUSIONS OF LAW

We conclude that Appellants have not demonstrated that the Examiner erred in combining the references to arrive at the claimed invention.

We thus affirm the rejection of claims 24, 26-32, and 36-40 under 35 U.S.C. § 103(a) as being obvious over the combination of Markovsky, Joris, and Litman, as well as the rejection of claims 34 and 35 under 35 U.S.C. § 103(a) as being obvious over the combination of Markovsky, Joris, and Litman, as further combined with Pall.

TIME LIMITS

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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